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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07K 1/02, 1/04, 1/107, 5/12, 7/64 — A1

(11) International Publication Number: WO 00/18790

(43) International Publication Date: 6 April 2000 (06.04.00)

(21) International Application Number: PCT/AU99/00813

(22) International Filing Date: 24 September 1999 (24.09.99)

(30) Priority Data:
PP 6164 25 September 1998 (25.09.98) AU

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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: SYNTHESIS OF CYCLIC PEPTIDES

(57) Abstract

This invention relates to methods for preparing cyclic peptides and peptidomimetic compounds in solution and bound to solid supports, and to cyclic peptide or peptidomimetic libraries for use in drug screening programmes. In particular the invention relates to a generic strategy for synthesis of cyclic peptides or peptidomimetics which enables the efficient synthesis under mild conditions of a wide variety of desired compounds. We have examined two approaches: 1) Positioning reversible *N*–amide substituents in the sequence. 2) Applying native ligation chemistry in an intramolecular sense. We have evaluated these for their improvements in the solution and solid phase synthesis of small cyclic peptides. We have systematically investigated the effects of preorganising peptides prior to cyclisation by using peptide cyclisation auxiliaries, and have developed new linkers to aid cyclic peptide synthesis. We have found surprising improvements in both yields and purity of products compared to the prior art methods. The combination of these technologies provides a powerful generic approach for the solution and solid phase synthesis of small cyclic peptides. We have also developed linkers and peptide cyclisation auxiliaries to aid cyclic peptide synthesis. The ring contraction and *N*–amide substitution technology of the invention provide improved methods for the synthesis of cyclic peptides and peptidomimetics. When used in conjunction with linker strategies, this combination provides solid–phase avenues to cyclic peptides and peptidomimetics.

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